Crouzon syndrome with acanthosis nigricans

Crouzon syndrome with acanthosis nigricans is a disorder characterized by the premature joining of certain bones of the skull (craniosynostosis) during development and a skin condition called acanthosis nigricans.

The signs and symptoms of Crouzon syndrome with acanthosis nigricans overlap with those of a similar condition called Crouzon syndrome. Both conditions involve premature fusion of the skull bones, which affects the shape of the head and face. Other common features of both conditions include wide-set, bulging eyes due to shallow eye sockets; eyes that do not point in the same direction (strabismus); a small, beaked nose; and a flat or sunken appearance of the middle of the face (midface hypoplasia). Less common features that can occur in either disorder include an opening in the roof of the mouth (cleft palate), dental problems, or hearing loss. People with Crouzon syndrome or Crouzon syndrome with acanthosis nigricans usually have normal intelligence.

Crouzon syndrome with acanthosis nigricans is distinguished from Crouzon syndrome by several features, including skin abnormalities. Acanthosis nigricans is a skin condition characterized by thick, dark, velvety skin in body folds and creases, including the neck and underarms. People with Crouzon syndrome with acanthosis nigricans may also have other skin abnormalities; for example, scars in the thick, dark areas of skin are flat and pale. These scars are usually from surgical procedures that are commonly needed in affected individuals. Additionally, in some people with the condition, one or both nasal passages are narrowed (choanal stenosis) or completely blocked (choanal atresia), which can cause difficulty breathing. A buildup of fluid in the brain (hydrocephalus) can also occur. Nasal passage abnormalities and hydrocephalus are rare in Crouzon syndrome. Less common features of Crouzon syndrome with acanthosis nigricans include subtle changes in the bones of the spine (vertebrae), abnormalities of the finger bones, and noncancerous growths in the jaw called cementomas.

Frequency

Crouzon syndrome with acanthosis nigricans is rare; this condition occurs in about 1 person per million. For unknown reasons, it affects females more than twice as often as males.

Genetic Changes

A mutation in the *FGFR3* gene causes Crouzon syndrome with acanthosis nigricans. This gene provides instructions for making a protein that is involved in the development

and maintenance of bone and other tissues. The genetic change involved in this disorder causes the FGFR3 protein to be overly active, which disrupts the normal growth of skull bones and affects skin pigmentation. These changes lead to the features of Crouzon syndrome with acanthosis nigricans.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

In some cases, an affected person inherits the mutation from one affected parent. More commonly, this condition results from new (de novo) mutations in the gene. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- CAN
- Crouzonodermoskeletal syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Crouzon syndrome with acanthosis nigricans
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2677099/

Other Diagnosis and Management Resources

- GeneReview: FGFR-Related Craniosynostosis Syndromes
  https://www.ncbi.nlm.nih.gov/books/NBK1455
- MedlinePlus Encyclopedia: Acanthosis Nigricans
  https://medlineplus.gov/ency/article/000852.htm
- MedlinePlus Encyclopedia: Craniosynostosis
  https://medlineplus.gov/ency/article/001590.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html

- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Acanthosis Nigricans
  https://medlineplus.gov/ency/article/000852.htm
- Encyclopedia: Craniosynostosis
  https://medlineplus.gov/ency/article/001590.htm
- Health Topic: Craniofacial Abnormalities
  https://medlineplus.gov/craniofacialabnormalities.html
- Health Topic: Skin Pigmentation Disorders
  https://medlineplus.gov/skinpigmentationdisorders.html

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Craniosynostosis Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Craniosynostosis-Information-Page

Educational Resources

- American Academy of Dermatology: Acanthosis Nigricans
  https://kidshealth.org/en/teens/acanthosis.html
- Center for Craniofacial Development and Disorders, Johns Hopkins Medicine: Craniosynostosis
  http://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/pediatric_neurosurgery/conditions/craniosynostosis/
- Disease InfoSearch: Crouzon syndrome with acanthosis nigricans
  http://www.diseaseinfosearch.org/Crouzon+syndrome+with+acanthosis+nigricans/8115
- KidsHealth from Nemours: Acanthosis Nigricans
  https://kidshealth.org/en/teens/acanthosis.html
- MalaCards: crouzon syndrome with acanthosis nigricans
  http://www.malacards.org/card/crouzon_syndrome_with_acanthosis_nigricans
- Orphanet: Crouzon syndrome-acanthosis nigricans syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=93262

- Seattle Children's Hospital and Regional Medical Center: Crouzon Syndrome
  http://www.seattlechildrens.org/medical-conditions/chromosomal-genetic-conditions/crouzon-syndrome/
- UC Davis Children's Hospital: Craniofacial Anomalies--Crouzon Syndrome
  https://www.ucdmc.ucdavis.edu/children/clinical_services/cleft_craniofacial/anomalies/crouzon.html

Patient Support and Advocacy Resources

- Children's Craniofacial Association
  http://www.ccakids.com
- Cleft Palate Foundation
  http://www.cleftline.org/parents-individuals/publications/crouzon-syndrome/
- Resource List from the University of Kansas Medical Center: Facial Anomalies/ Craniofacial Conditions
  http://www.kumc.edu/gec/support/craniofa.html

GeneReviews

- FGFR-Related Craniosynostosis Syndromes
  https://www.ncbi.nlm.nih.gov/books/NBK1455

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Crouzonodermoskeletal+syndrome%22+OR+%22Craniofacial+Dysostosis%22+OR+%22Crouzon%27s+Disease%22+OR+%22Crouzons+Disease%22+OR+%22Craniosynostosis%22+OR+%22Crouzon+Disease%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28crouzonodermoskeletal+syndrome%29+OR+%28crouzon+syndrome+with+acanthosis+nigricans%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- CROUZON SYNDROME WITH ACANTHOSIS NIGRICANS
  http://omim.org/entry/612247

Sources for This Summary

- Arnaud-López L, Fragoso R, Mantilla-Capacho J, Barros-Núñez P. Crouzon with acanthosis nigricans. Further delineation of the syndrome. Clin Genet. 2007 Nov;72(5):405-10.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17935505
- Chen F, Degnin C, Laederich M, Horton WA, Hristova K. The A391E mutation enhances FGFR3 activation in the absence of ligand. Biochim Biophys Acta. 2011 Aug;1808(8):2045-50. doi: 10.1016/j.bbamem.2011.04.007.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21536014
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3110564/
- Chen F, Sarabipour S, Hristova K. Multiple consequences of a single amino acid pathogenic RTK mutation: the A391E mutation in FGFR3. PLoS One. 2013;8(2):e56521. doi: 10.1371/journal.pone.0056521.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23437153
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3577887/
- Cohen MM Jr. Let's call it "Crouzonodermoskeletal syndrome" so we won't be prisoners of our own conventional terminology. Am J Med Genet. 1999 May 7;84(1):74.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10213050
- GeneReview: FGFR-Related Craniosynostosis Syndromes
  https://www.ncbi.nlm.nih.gov/books/NBK1455
- Mir A, Wu T, Orlow SJ. Cutaneous features of Crouzon syndrome with acanthosis nigricans. JAMA Dermatol. 2013 Jun;149(6):737-41. doi: 10.1001/jamadermatol.2013.3019. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23571469
- Schweitzer DN, Graham JM Jr, Lachman RS, Jabs EW, Okajima K, Przylepa KA, Shanske A, Chen K, Neidich JA, Wilcox WR. Subtle radiographic findings of achondroplasia in patients with Crouzon syndrome with acanthosis nigricans due to an Ala391Glu substitution in FGFR3. Am J Med Genet. 2001 Jan 1;98(1):75-91.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11426459
- Vajo Z, Francomano CA, Wilkin DJ. The molecular and genetic basis of fibroblast growth factor receptor 3 disorders: the achondroplasia family of skeletal dysplasias, Muenke craniosynostosis, and Crouzon syndrome with acanthosis nigricans. Endocr Rev. 2000 Feb;21(1):23-39. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10696568

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/crouzon-syndrome-with-acanthosis-nigricans

Reviewed: March 2017
Published: April 25, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services